

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Withdrawn) A method of evaluating a compound for a modulatory effect on a disorder, the method comprising:
  - a) providing a library of compounds;
  - b) contacting each compound of the library to a GH/IGF-1 axis component or a functional fragment thereof, *in vitro*;
  - c) evaluating interaction between each compound and the GH/IGF-1 axis component;
  - d) selecting a subset of compounds from the library based on the evaluated interactions;
  - e) contacting a compound of the subset to (i) a cell *in vitro*, the cell being from a subject having the disorder or from non-human animal model of the disorder, or (ii) a non-human animal model of the disorder; and
  - f) evaluating the cell or the animal model, wherein a change in a parameter of the disorder identifies the respective compound as having a modulatory effect on the disorder.
2. (Withdrawn) The method of claim 1 wherein contacting the compound to the animal model comprises administering the compound to the animal model.
3. (Withdrawn) The method of claim 1 wherein the disorder is a neoplastic disorder, a neurological disorder, other than a disorder caused by polyglutamine aggregation, a metabolic disorder, an immunological disorder, a tissue repair condition, a dermatological disorder, a dermatological tissue condition, or a cardio-vascular disorder.

4. (Withdrawn) The method of claim 1 wherein the disorder is Alzheimer's, Parkinson's, ALS, skeletal muscle atrophy, multiple sclerosis, a neuropathy, age-related macular degeneration, diabetic retinopathy, or non-insulin-dependent diabetes.

5. (Withdrawn) The method of claim 1 wherein the component is a cell surface receptor or secreted molecule.

6. (Withdrawn) A method of evaluating a compound for a modulatory effect on a disorder, the method comprising:

- a) selecting a GH/IGF-1 axis modulator;
- b) contacting the modulator to (i) a cell in vitro, the cell being from a subject having the disorder or from non-human animal model of the disorder, or (ii) a non-human animal model of the disorder; and
- c) evaluating the cell or the animal model, wherein a change in an parameter of the disorder identifies the respective compound as having a modulatory effect on the disorder, wherein the disorder is selected from the group consisting of: an immunological disorder, a dermatological disorder, a dermatological tissue condition, a cardio-vascular disorder, or a neurological disorder, other than a neurological disorder caused by polyglutamine aggregation.

7. (Withdrawn) The method of claim 6 wherein the modulator is a compound that directly antagonizes a positively acting GH/IGF-1 axis component.

8. (Withdrawn) The method of claim 6 wherein the modulator is a compound that directly agonizes an inhibitory GH/IGF-1 axis component.

9. (Withdrawn) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

- a) providing a test compound;

b) contacting the test compound to a GH/IGF-1 axis component *in vitro*;  
c) evaluating interaction between the test compound and the GH/IGF-1 axis component;  
d) administering the test compound to an adult, non-human subject; and  
e) evaluating an age-associated parameter of the adult subject, wherein an interaction between the test compound the GH/IGF-1 axis component and modulation of the age-associated parameter relative to a control subject identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

10. (Withdrawn) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

a) providing a library of compounds;  
b) contacting each compound of the library to a GH/IGF-1 axis component *in vitro*;  
c) evaluating interaction between each compound and the GH/IGF-1 axis component;  
d) selecting a subset of compounds from the library based on the evaluated interactions;  
e) administering (e.g., individually) each compound of the subset to an adult, non-human subject; and  
f) evaluating an age-associated parameter of the adult subject, wherein modulation of the age-associated parameter relative to a control subject identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

11. (Withdrawn) The method of claim 10, wherein the age-associated parameter comprises one or more of:

- (i) lifespan of the subject, or a cell in the subject;
- (ii) presence or abundance of a gene transcript or gene product that has a biological age-dependent expression pattern in a cell of the subject;
- (iii) resistance of the subject or a cell of the subject to stress;
- (iv) one or more metabolic parameters of the subject or a cell of the subject ; and
- (v) proliferative capacity of a cell of the subject.

12. (Withdrawn) The method of claim10, wherein the *in vitro* contacting is a cell-based assay.

13. (Withdrawn) The method of claim10, wherein the *in vitro* contacting is a cell-free assay.

14. (Withdrawn) The method of claim10, wherein the adult subject is a non-human mammal.

15. (Withdrawn) The method of claim10, wherein the subject has normal IGF-1 levels.

16. (Withdrawn) The method of claim10, the GH/IGF-1 axis component is a cell surface receptor.

17. (Withdrawn) The method of claim10, the GH/IGF-1 axis component is a pre-IGF1 component.

18. (Withdrawn) The method of claim10, the GH/IGF-1 axis component is a post-IGF1 component.

19. (Withdrawn) The method of claim 10 wherein the library comprises multiple compounds that have a molecular weight less than 7000 Daltons.

20. (Withdrawn) The method of claim 10 wherein the library comprises one or more of an immunoglobulin, a peptide, a nucleic acid aptamer, a dsRNA, a siRNA, a ribozyme, or an antisense nucleic acid.

21. (Withdrawn) The method of claim 10 wherein each compound of the library is non-polymeric.

22. (Withdrawn) The method of claim 10 further comprising formulating an identified compound as a pharmaceutical composition.

23. (Withdrawn) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

- a) providing a test compound;
- b) contacting the test compound to a GH/IGF-1 axis component *in vitro*;
- c) evaluating interaction between the test compound and the growth hormone/IGF-1 axis component;
- d) contacting the test compound to a cell; and
- d) evaluating an age-associated parameter of the cell, wherein an interaction between the test compound the GH/IGF-1 axis component and modulation of the age-associated parameter relative to a control cell identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

24. (Withdrawn) The method of claim 23, wherein the age-associated parameter comprises one or more of:

- (i) lifespan of the cell;
- (ii) presence or abundance of a gene transcript or gene product that has a biological age-dependent expression pattern in the cell;
- (iii) resistance of the cell to stress;
- (iv) one or more metabolic parameters of the cell ;
- (v) proliferative capacity of the cell ; and
- (vi) physical appearance or behavior of the cell.

25. (Currently amended) A method of identifying a GH/IGF-1 axis antagonist ~~or partial agonist~~, the method comprising:

a) providing a ~~test compound~~ small molecule that is obtained by chemically modifying an agonist of a ~~GH/IGF-1 axis component~~ GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 or that is selected for structural similarity to an agonist of an ~~GH/IGF-1 axis component~~ GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3; and

b) evaluating a ~~property activity~~ of a ~~GH/IGF-1 axis component~~ GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 *in vitro*, in a cell, or in an organism in the presence of the ~~test compound~~ small molecule, wherein ability of the ~~test compound to modulate the property~~ small molecule to antagonize the activity of the ~~GH/IGF-1 axis component~~ GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 identifies the ~~compound~~ small molecule as a ~~GH/IGF-1 axis~~ GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 antagonist.

26. (Original) The method of claim 25 wherein the evaluating comprises a cell-free assay or a cell-based assay.

27. (Currently amended) The method of claim 25 wherein the evaluating comprises administering the ~~test compound~~ small molecule to an adult organism.

28. (Original) The method of claim 27 wherein the organism has normal IGF-1 levels prior to the administering.

29. (Currently amended) The method of claim 27 wherein a cohort of adult ~~organism~~ organisms are treated and evaluated, each organism of the cohort characterized by normal IGF-1 levels prior to the treating.

30. (Currently amended) The method of claim 27 wherein the evaluating comprises evaluating GH or IGF-1 levels, and decreased levels of growth hormone and/or IGF-1 identifies the ~~test compound~~ small molecule as an ~~agent or modulator~~ antagonist.

31. (Cancelled)

32. (Withdrawn) The method of claim 25 further comprising d) evaluating an age-associated parameter of a subject treated with the test compound, wherein modulation the age-associated parameter relative to a control subject further identifies the test compound as an agent that modulates lifespan regulation or potential.

33. (Withdrawn) A method of identifying an agent that modulates lifespan regulation of an adult animal, the method comprising

- a) selecting an agent that alters a property of GH/IGF-1 axis;
- b) administering the agent to a subject; and
- c) evaluating an age-associated parameter in the subject, wherein modulation of the age-associated parameter identifies the agent as an agent that modulates lifespan regulation or potential.

34. (Withdrawn) The method of claim 33 wherein the agent is a direct antagonist of a positively acting component of the GH/IGF-1 axis.

35. (Cancelled)

36. (Currently amended) The method of claim 25, wherein the ~~test compound~~ small molecule is combined with a pharmaceutically acceptable carrier.